GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF RESEARCH ADMINISTRATION

RESEARCH PROJECT INITIATION

Date: May 28, 1974

Project Title: Byssinosis and Small Airways Disease

Project No: C-10-621

Principal Investigator: Dr. James M. Bradford

Sponsor: Public Health Service

Agreement Period: From May 1, 1974 Until April 30, 1975

Type Agreement: Grant Number 1 R01 OH 00460-01 SOH

Amount:
$76,882 PHS
4,046 Tech Cost-sharing (C-10-316)
$80,928 Total

Reports Required: Annual Progress; submitted with renewal.
Final Progress; if project is not renewed.

Sponsor Contact Person (s):
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Assigned to: OIP

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RA-3 (6-71)

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION

Date: September 30, 1976

Project Title: Byssinosis and Small Airways Disease

Project No: C-10-621

Project Director: Dr. James M. Bradford

Sponsor: Public Health Service

Effective Termination Date: 4/30/76

Clearance of Accounting Charges: 4/30/76

Grant/~~Contract~~ Closeout Actions Remaining: None

_ Final Invoice and Closing Documents
_ Final Fiscal Report
_ Final Report of Inventions
_ Govt. Property Inventory & Related Certificate
_ Classified Material Certificate
_ Other _____

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CA–4 (3/76)

TERMINAL PROGRESS REPORT

GRANT NUMBER:	OH 00460-01
PERIOD COVERED:	1 May, 1974 to 1 May, 1976
PRINCIPAL INVESTIGATOR:	James M. Bradford, Jr., Ph.D.
INSTITUTION:	Georgia Institute of Technology
TITLE:	Byssinosis and Small Airways Disease

SUMMARY:

The project was moved from Georgia Institute of Technology to Emory University during the third grant year, so this final report covers the initial two years of the project. The data-gathering phase is proceeding as expected with no delays expected in the completion of the project during the final year at Emory University. The equipment is working well with reliable and accurate data being gathered. The data analysis phase of the project is just beginning.

A. INTRODUCTION

1. General

The original grant that started this project was awarded to the Georgia Institute of Technology (OH 00460-01) starting 1 May, 1974, for a period of three years. At the end of the second year of the grant; however, the principal investigator left the Georgia Institute of Technology and took a position at Emory University. In order to complete the work to be done, the original grant with Georgia Institute of Technology was terminated and a one-year grant awarded to the principal investigator at Emory University. The present final report is then a final report of the work done while at Georgia Institute of Technology and thus is for the two years of work done there. Because of the large number of subjects to be tested and the statistical interpretation of the results, the final data analysis is scheduled to be done during the present year. This report will, then, necessarily contain information other than the data analysis.

2. Objective

The long term goals of the proposed research are 1) to investigate the relationship between small airways disease and cotton dust exposure in a non-byssinotic population, 2) to correlate the incidence of small airways disease with respirable dust levels in a cotton textile mill, and 3) to estimate the site of the obstruction (large versus small airways) in a byssinotic population.

3. Background

All of the current tests for the determination of the objective symptoms of byssinosis rely upon some decrease in forced expiratory flow as the disease indicator. It has been shown that at some stage byssinosis may lead to irreversible chronic obstructive pulmonary disease (COPD). A question that has not been answered is the way in which byssinosis develops into COPD and at what stage of byssinosis irreversible lung damage occurs. A certain amount of irreversible damage may have already occurred at the time that byssinosis can be diagnosed using current testing methods. Thus, a more sensitive test for the onset of airway obstruction is desirable. One possible more sensitive test is the test for small airways disease.

The concept of small airways disease is important in helping to understand some uncommon and yet perplexing clinical syndromes and has aided in the understanding of disproportionately severe ventilation-perfusion abnormalities with only moderate increases in airway resistance. Perhaps more importantly, small airways disease might be the earliest lesion (possibly reversible) in the development of COPD.

Small airways disease has been demonstrated in early bronchitis (1) and asymptomatic asthmatics (1) and in asymptomatic smokers (2). Studies of small airways disease in relation to cotton dust exposure could lead to a better understanding of byssinosis. The questions to be answered are: Is byssinosis due to involvement of both large and small airways or is it confined to only large airways? Do workers develop small airway abnormalities before the onset of large airway obstruction? Are any of the small airway abnormalities reversible, and if so, under what conditions? Can the presence of small airways abnormalities be used to predict the onset of a chronic obstructive syndrome? At what dust levels do small airways disease develop?

B. SPECIFIC AIMS

1. Determine the incidence of small airway abnormalities (episodic and chronic) in a non-byssinotic population of cotton mill workers.

2. Determine the contribution of large versus small airway obstruction to flow limitation in the byssinotic population.

3. Determine the relationship of respirable cotton dust levels and both small airways abnormalities and large airway obstructions.

4. Examine the relationship between acute symptoms in that portion of the population with no decrease in $FEV_{1.0}$ after cotton dust exposure and the incidence of small airway abnormalities.

C. METHODS AND EQUIPMENT

1. Population

In order to be able to have any statistical confidence in the results we determined that 600 subjects will be tested. 200 subjects will be from high dust areas (opening, picking, carding), 200 from low dust areas (spinning to weaving) and 200 controls from offices and warehouses.

2. Equipment

a. Mobile Pulmonary Laboratory

In order to test this many subjects efficiently, all of the equipment is mounted in a 30-foot long mobile pulmonary laboratory. The laboratory is completely self-contained and needs no external electrical or other utility connections. Inside the van are two pressure corrected pressure-volume plethysmographs connected to a DEC PDP8-E minicomputer. Electrical power is provided by two 110 volt generators. The 6KW generator provides power for the air conditioners and other auxillary devices, and the 4KW generator provides power for the computer and instruments. A constant voltage transformer controls the voltage to the computer circuit. Leveling jacks are provided under the van to stabilize it when parked and the two generators are jacked off their van supports so that they are supported from the ground during testing.

b. Plethysmographs

The plethysmographs are similar in design with the one in the rear of the van being slightly larger for larger subjects. The one in the front of the van measures 26" wide, $22\frac{1}{2}$" deep and $56\frac{1}{2}$" high. The one in the rear is 28" wide, $24\frac{1}{2}$" deep, and $58\frac{1}{2}$" high. The doors are plexiglas and a plexiglas window is in front of the subject sitting in the plethysmograph. The mouthpiece holder is a piece of flexible rubber tubing which leads through the window to a shutter and a low resistence two-way valve. The inlet side of the valve is switched to either air or a helium-oxygen mixture by a manual valve. The outlet side of the two-way valve goes to a "bag in a box" arrangement with the flowmeter measuring the flow out of the box. The bag is emptied periodically by a suction line from a vacuum cleaner. A laminar flow screen is mounted in the wall of each of the plethysmographs to measure the flow in and out of the plethysmograph. The mouth pressure is measured by a pressure transducer attached to the pressure tap on the mouth shutter. Pressure transducers also measures the pressure drops across the #4 Fleish head in the "bag in the box" apparatus and across the laminar flow screen in the wall of the plethysmograph.

c. Computer

The analog signals from the mouth pressure and mouth flow transducer amplifiers go directly to the analog to digital converter in the computer. The plethysmograph flow signal is integrated and part of the flow signal is added to the integrated flow signal. In this way the plethysmograph can be "tuned" to increase the frequency response of the plethysmograph volume signal. The integrated plethysmograph flow signal is then sent to the computer.

The test procedure is controlled by a console adjacent to each plethysmograph. The console contains a keyboard and a storage oscilloscope which are interfaced with the computer and a manual control box for manually controlling the test. Using the keyboard as the input device and the storage oscilloscope as the output device, the pulmonary function testing procedure is controlled by the technician using the computer. The detailed test protocol is discussed below.

The computer is a DEC PDP8-E with eight channels of A/D conversion, dual tape

drives, 16K of core memory, and a customized interface for the scopes, keyboards, and eight relay controls. The computer operates in a time-sharing mode so that either or both of the plethysmographs may be taking or displaying data at any time and testing can take place simultaneously in both plethysmographs.

d. Calibration Syringe

A special calibration syringe was constructed with a volume of about 4 liters. This piston-type device is driven by a constant speed motor so that the flow output is a known wave shape. Thus when the output of the syringe is directed into either of the plethysmographs, the known volume and peak flow signal from the syringe is used to calibrate the flow transducers. The mouth pressure transducer is calibrated using a water manometer. The calibrating flow and volume signals are processed by the computer so that when a calibration is conducted the entire system from pressure transducer to computer output is calibrated.

e. Vertical Elutriator

Vertical Elutriators are used to measure the repirable dust levels. The filters are weighed with a microbalance before the trip is started and are installed in the elutriators and the elutriators started about thirty minutes before the work shift starts. The filters are changed at the end of the work shift. The filters are not weighed until the trip is over.

3. Protocol

a. Pretest

On the day before the testing is to be done the equipment is all checked out and a pretest check list is completed. This insures that all of the supplies needed are present and that all of the equipment is working properly. The consent forms and medical questionnaires would have been filled out on a previous visit. The testing team consisting of the principal investigator and three technicians travel to the testing site on Sunday afternoon prior to the testing. The mobile pulmonary laboratory is set up and the equipment is again checked out and calibrated. Another pretest check list is completed to insure that all of the calibrations are performed and properly recorded.

The testing team returns to the van about one hour before the subjects are to arrive and turns the equipment on and allows it to warm up. After the equipment has warmed up another calibration is conducted.

b. Test Procedure

The subjects start arriving about one hour before their Monday work shift begins and the testing begins at that time. It usually continues until about 30 minutes after their work shift should have begun and, of course, the subjects do not enter the mill until after they are tested. They are retested starting five hours after their work shift and it usually takes only about an hour to retest everyone. An average of about twelve subjects per shift are tested and two work shifts are tested on each plant visit.

Upon entering the van the subjects are instructed as to what is expected of them in the test procedure and then asked to sit in the plethysmograph and breath through the mouthpiece. A nose clip is used on each subject. While the subject is becoming acclimated to the plethysmograph a short form is filled out on each subject and identification information is entered into the computer. The subject is then instructed to pant gently at which time the mouth shutter occludes the airway and the information to determine the thoracic gas volume (TGV) is measured. As soon as the shutter opens the subject is then coached to exhale as much as possible. The computer then measures the change in volume from the shutter opening to the end of the exhalation and subtracts this exhaled volume from the TGV to give the residual volume (RV). This maneuver is repeated until three successful RV determinations have been made. After each maneuver the raw data is recorded on the digital tape drive. The subject is then coached to inhale as much as possible and to exhale vigorously and completely until no more air can be exhaled. During this time the computer displays the maximum expiratory flow volume maneuver and

the various derived pulmonary parameters for evaluation by the technician. If this test is valid it is then recorded on the tape and this MEFV maneuver is repeated until three valid tests have been recorded.

During all the previous testing the subject has been breathing air. At this point in the testing the manual valve controlling the air supply to the subject is switched so that the subject is breathing a 80% helium-20% oxygen mixture. The subject is instructed to perform at least three slow maneuvers in which they fill their lungs completely with helium and then exhale as much as possible. After this the subject performs three MEFV maneuvers on the helium-oxygen mixture and the data is recorded. The subject is then switched back to breathing air and asked to breath normally until the helium has been washed out of the lungs. The subject is then asked to exit the plethysmograph which ends the test. A written log or summary of each test is written down as each subject is tested so that there is a summary of each subject's performance kept at the time of testing.

c. Post Test

After the subjects have all been tested after having been on the job for five hours, the calibration procedure is again conducted for both plethysmographs. The appropriate calibration results and scale factors are recorded and the van is then readied for the trip back to Emory.

After returning, the raw data from each test from each subject is reviewed using the computer by a program which allows the technician to intervene if the program did not choose the correct values on the various curves. A summary of the parameters from each test is then written onto another tape for eventual transfer to the larger computer at the Emory University Computer Center. The data is next evaluated by a program which chooses the "best" test from each of the subject's tests. Thus, there will be only one "best" test for breathing air and one for helium before going on the job, and another set of "best" tests after being on the job for five hours. The criterion for the "best" test is still being developed but is based largely upon the work of Palmer (3) and will choose in general the test with the largest vital capacity if the FEV_1 of that test is not considerably lower than the FEV_1 of another test.

After the four "best" tests are chosen, they are passed to an information management system known as GIPSY which allows easy manipulation of the data for study.

D. RESULTS

So far a total of approximately 300 subjects have been tested in 13 trips. The testing is still going on but should be completed by October, 1976. The data analysis has already begun, but the number of subjects' data transferred to the Emory University Computer at this time is not large enough for any significant results.

We have studied over results to determine how repeatable our results are and the average difference between the two largest vital capacities is slightly less than 5% and the average difference between the FEV_1's for the same two tests is about 4%.

REFERENCES:

1. Levine, G., et al.: Gas exchange abnormalities in mild bronchitis and asymptomatic asthma. New Eng. J. Med., 282:1277-1282, 1970.

2. Ingram, R.H., Jr., and O'Cain C.F.: Frequency dependence of compliance in apparently healthy smokers versus non-smokers. Bull. Physio-path. Resp. 7:195-212, 1971.

3. Discher, D.P., and Palmer, A.H.: Development of a New Motivational Spirometer - Rationale for Hardware and Software. J. Occup. Med., 14:679-685, 1972.